

In re Appln. of Westbrook *et al.*
Application No. 09/897,798
Attorney Docket No. 21726/92526

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph starting on page 7, at line 4, through line 14, with the following:

Human cDNA filter arrays were used to establish the expression profiles for both species, because there is no comparable product available for baboon cDNA analysis, and a high nucleotide sequence homology between these two species was expected (Liao *et al.*, 1998; Trezise *et al.*, 1989). The cDNA filter arrays used (GeneFiltersTM) contained 25,920 cDNAs from the UniGene dataset (<http://www.ncbi.nlm.nih.gov/UniGene/index.html>) (National Center for Biological Information UniGene Collection), including both known genes and uncharacterized ESTs, permitting the survey of one-fourth to one half of the estimated 50,000-100,000 genes in the genome. The transcriptosome of CD34⁺ cells, is disclosed herein, demonstrating very comparable gene expression patterns in CD34⁺ cells in these two species, and validating the utility of human cDNA arrays for baboon studies.

Please replace the paragraph beginning on page 8, line 26, through page 9, line 5 with the following:

Genes from this database were then ranked from highest to lowest level of expression, as determined from their measured intensity in human CD34+ RNA. The rank order is only approximate, because the filters cannot provide the absolute level of expression, and there is experimental error in taking the measurements, but confirmatory experiments for randomly-selected genes have shown a fairly good correlation with rank order and expression measured by other methods. Additions, or corrections to the list may be made within the scope of the

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invention, but the underlying concept and the majority of the listed genes are as indicated herein. The complete gene list is appended as Appendix A and is available through a web site <http://westsun.hema.uic.edu/html/expression.html> which will be available to the public upon filing the present patent application. Table 2 shows selective highly-abundant EST's and partially characterized cDNAs in human an baboon CD34+ cells.

Please replace the paragraph on page 9, starting at line 6, through line 11, with the following:

The gene filters which were used to identify the genes are commercially available from Research Genetics, but any filter array might have been used. The genes themselves are selected from databases that are in the public domain (UniGene dataset), <http://www.ncbi.nlm.nih.gov/UniGene/index.html> as part of the Human Genome Program. The invention is to compile a specialized database using the criteria herein for applications involving hematopoiesis.

Please replace the paragraph beginning on page 9, line 12, through line 22, with the following:

The genes defined in this invention are represented as UniGene cluster numbers. UniGene (<http://www.ncbi.nlm.nih.gov/UniGene/index.html>) is a product of the Human Genome Program, maintained by the National Center for Biotechnology Research. UniGene contains over 40,000 entries, each of which represents a unique gene based on a composite of sequences of individual clones from cDNA libraries. The cDNA clones represented in UniGene are

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available for purchase from a number of repositories, including TIGR (The Institute For Genome Research, <http://www.tigr.org/tdb/tdb.html>). The dataset and representative clones are publicly available to any investigators, but the clones specified by this invention, and their association as a group with bone marrow and related cell types, and their expression levels, are not publicly available data.

Please replace the paragraph beginning on page 15, line 19, through line 32, with the following:

Radioactively-labeled RNA-based probes prepared from each cellular population were hybridized to five nylon filter membrane arrays (GeneFilters releases 200-204, containing a total of 25,920 cDNAs) and phosphoimaged, and the resultant image was analyzed to determine the relative hybridization signal intensity for each cDNA with each probe. Each cDNA on the array is derived from a single clone from the IMAGE (Integrated Molecular Analysis of Genomes and their Expression) consortium at Lawrence Livermore National Laboratory (Livermore, CA) (<http://image.llnl.gov>) representing the 3'-end of a unique UniGene cluster. All data were obtained by sequential hybridization to a single filter set, in order to provide the most accurate comparisons between probes and avoid variability in cDNA spotting. Duplicate experiments were performed when possible, but were limited by the lifetime of the filters, which in general could be successfully re-hybridized no more than 3 to 4 times. It was not possible to use pooled baboon marrow donors because of the limited availability of animals, and thus pooled human donors were not used either, recognizing that the methods of the present invention are not sensitive enough to detect small differences between individual donors.

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Please replace the paragraph beginning on page 16, line 1, through line 15 with the following.

Normalized signal intensities for individual cDNA spots from these hybridizations were compared by scatter analysis, and revealed that the gene expression patterns in human and baboon cells were very similar, with an overall correlation of 0.87. The composite data for all hybridizations is summarized on a scatter plot (FIG. 1). The measured raw intensity of the hybridization signal relative to the filter background is used as an indicator of the relative abundance of the cDNA. For these experiments, a cut-off level of raw intensity (non-normalized) of 3-fold over background was used to indicate that a gene is definitively expressed in human cells. By this criteria, human CD34⁺ cells displayed positive expression for approximately 15,970 (62%) of the 25,920 cDNAs present on these filters. This gene list excludes many housekeeping genes, which are measured on the GeneFilters as hybridization controls but are not included for normalization by Pathways II software. (For information on all the spotted cDNA for each filter including the housekeeping genes, refer to the Research Genetics, Huntsville, AL). Genetics's ftp website, <ftp://ftp.resgen.com/pub/genefilters/>).

Please replace the paragraph beginning on page 17, line 3, through line 17, with the following paragraph:

The very highly-abundant genes identified by Pathways II analysis were then updated to the most current UniGene release (version 118, April 2000), and examined in detail. A total of 1,554 UniGene clusters remained after updating. This list included 595 named genes, and 959

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ESTs and uncharacterized cDNAs. This list of highly-abundant genes and ESTs is available as an appendix to the online version of this article, ~~and is also available on our hematopoietic stem cell website (<http://westsun.hema.uic.edu/html/expression.html>)~~. The named genes represent a wide variety of functional categories such as growth factors and cytokines, receptors and cell surface molecules, intracellular signalling molecules, cell cycle proteins etc. A sample of these genes, sorted by functional category, are given in Table 1. Note that this list includes many of the genes (typed in bold) that would be expected to be present in CD34⁺ cells, such as receptors for IL3 and colony stimulating factor 3. Interestingly, many expected hematopoietic genes are not in this category, as their level of expression is relatively low; for example, the CD34 antigen is expressed at a relatively low level, only 6-fold above background (for human).